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1883474 METHYL?/BI 1006410 METHYL?/AB

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90004 GASTRIC?/BI                79881 GASTRIC?/AB
117491 STOMACH?/BI               51390 STOMACH?/AB
0 CANCEER?/BI                    0 CANCEER?/AB
193324 CARCINOMA?/BI             129532 CARCINOMA?/AB
9304 DYSPLAS?/BI                 8183 DYSPLAS?/AB
550132 NEOPLAS?/BI               52223 NEOPLAS?/AB
522879 TUMOR?/BI                 436083 TUMOR?/AB
5241 TUMOUR?/BI                  121 TUMOUR?/AB
L1      343 (CPG AND METHYL? AND (GASTRIC? OR
STOMACH?) AND (CANCEER? OR       CARCINOMA? OR
DYSPLAS? OR NEOPLAS? OR TUMOR? OR TUMOUR?))/BI,AB

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L2      316 L1 NOT 2008/PY

=> s l2 not 2007/py   1624680 2007/PY
L3      264 L2 NOT 2007/PY

=> s l3 not 2006/py   1542663 2006/PY
L4      212 L3 NOT 2006/PY

=> s l4 not 2005/py   1408138 2005/PY
L5      172 L4 NOT 2005/PY

=> s l5 not 2004/py   1331664 2004/PY
L6      121 L5 NOT 2004/PY

=> s p16/bi,ab        5236 P16/BI                4719 P16/AB
L7      5236 P16/BI,AB

=> s l6 and l7
L8      19 L6 AND L7

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L2      316 S L1 NOT 2008/PY
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L5      172 S L4 NOT 2005/PY
L6      121 L5 NOT 2004/PY
L7      5236 S P16/BI,AB
L8      19 S L6 AND L7

=> d l8 1-19 bib ab

L8  ANSWER 1 OF 19  CAPLUS  COPYRIGHT 2008 ACS on STN
AN  2003:833358  CAPLUS <<LOGINID::20080705>>
DN  140:3437
TI  Aberrant  ***CpG***  island hypermethylation of chronic
gastritis, in relation to aging, gender, intestinal metaplasia, and
chronic inflammation
AU  Kang, Gyeong Hoon; Lee, Hyeon Joo; Hwang, Kyu Sang;
Lee, Sun; Kim, Jae-Hoon; Kim, Jung-Sun
CS  Department of Pathology and Cancer Research Institute,
Seoul National University College of Medicine, Seoul, S. Korea
SO  American Journal of Pathology (2003), 163(4), 1551-1556
CODEN: AJPAA4; ISSN: 0002-9440
PB  American Society for Investigative Pathology
DT  Journal
LA  English
AB  Aberrant hypermethylation of promoter  ***CpG***
islands is an important mechanism for the inactivation of
***tumor***  suppressor genes.  ***CpG***  island
hypermethylation occurs in relation to  ***tumorigenesis***  or
aging.  ***Gastric***  cancer is one of the  ***tumors***
with a high level of aberrant  ***CpG***  island
***methylation***  . However, the data on the
***methylation***  status of normal  ***gastric***  mucosa
was very limited. The present study attempted to compare the
***methylation***  status of nonneoplastic  ***gastric***
mucosa, using clinicopathol. parameters, including age, gender,
Helicobacter pylori (H. pylori), acute and chronic inflammation,
and intestinal metaplasia. Two hundred sixty-eight nonneoplastic
***gastric***  mucosa samples were studied for the
***methylation***  status of 11 genes (COX-2, DAP-kinase, E-
cadherin, GSTP1, MGMT, hMLH1, p14,  ***p16***  , THBS1,
TIMP3, and RASSF1A), using  ***methylation***  -specific PCR.
***CpG***  island hypermethylation was found in 53.7, 41,
37.7, 23.1, 18.7, 10.9, 10, 4.1, 3.4, 1.7, 0.4% for DAP-kinase, E-
cadherin, THBS1, TIMP3, p14, MGMT,  ***p16***  , COX-2,
GSTP1, hMLH1 and RASSF1A, resp. Five genes (DAP-kinase, E-
cadherin, p14, THBS1, and TIMP-3) showed a general
progressive increase in the  ***methylation***  frequency as a
function of aging, whereas the other genes (COX-2, GSTP1,
MGMT, hMLH1,  ***p16***  , and RASSF1A) were rarely
***methylated***  . Male patients showed higher nos. of
***methylated***  genes than females (3.2 vs. 2.1, resp., P =
0.002). Gastritis samples with marked intestinal metaplasia,
showed higher nos. of genes  ***methylated***  than those
without (3.7 vs. 2.6, resp., P = 0.021). Gastritis samples with
marked infiltration of mononuclear cells displayed higher nos. of
genes  ***methylated***  than those with mild or moderate
infiltration of mononuclear cells (3.4 vs. 2.5 or 2.5, resp., P <
0.05). Our results demonstrated that many genes are
***methylated***  in the  ***stomach***  as a function of
age, and suggested that male gender, intestinal metaplasia, and
chronic inflammation are closely associd. with increased
***methylation***  in nonneoplastic  ***gastric***  mucosa
samples.
RE.CNT  37  THERE ARE 37 CITED REFERENCES AVAILABLE
FOR THIS RECORD  ALL CITATIONS AVAILABLE IN THE RE
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L8  ANSWER 2 OF 19  CAPLUS  COPYRIGHT 2008 ACS on STN
AN  2003:616883  CAPLUS <<LOGINID::20080705>>
DN  139:271591
TI  Detection of  ***methylation***  of human p16Ink4a gene
5'-  ***CpG***  islands by electrochemical method coupled with
linker-PCR
AU  Hou, Peng; Ji, Meiju; Ge, Cunwang; Shen, Jiayao; Li, Song;
He, Nongyue; Lu, Zuhong
CS  Department of Biological Science and Medical Engineering,
Chien-Shiung Wu Laboratory, Southeast University, Nanjing,
210096, Peop. Rep. China
SO  Nucleic Acids Research (2003), 31(16), e92/1-e92/7 CODEN:
NARHAD; ISSN: 0305-1048
PB  Oxford University Press
DT  Journal
LA  English
AB  Aberrant DNA  ***methylation***  of the  ***CpG***
site is among the earliest and most frequent alterations in cancer.
Detection of promoter hypermethylation of cancer-related genes
may be useful for cancer diagnosis or the detection of
recurrence.  ***p16***  , an inhibitor of the cyclin D-dependent
protein kinases, is a classical  ***tumor***  suppressor gene,
and its inactivation is closely assocd. with carcinogenesis.
***P16***  hypermethylation could be detected in each stage,
which is consistent with the finding that aberrant
***methylation***  of  ***p16***  is a very early event in
```

carcinogenesis. We have developed an electrochem. procedure for detecting DNA ***methylation*** of the human p16Ink4a gene. The procedure is based on the coupling of DNA electrochem. sensors with linker-PCR- amplified DNA from human ***gastric*** ***tumor*** tissue and whole blood cells of healthy human. The synthesized oligonucleotide was immobilized on the modified gold electrode to fabricate a DNA biosensor. The hybridization reaction on the electrode surface was monitored by cyclic voltammogram (CV) and square wave voltammogram (SWV), using [Co(phen)3](CO4)3 as a redox indicator. ***Methylation*** status of human p16Ink4a gene was detected and the results were validated by bisulfite DNA sequencing. A good reproducibility was obsd. in several parallel expts. The coupling of DNA electrochem. sensors with PCR allowed quick detection and have the potential of the quant. evaluation of the ***methylation*** status of the human p16Ink4a gene.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:480615 CAPLUS <<LOGINID::20080705>>
DN 139:195353
TI Age-related ***methylation*** of ***tumor*** suppressor and ***tumor*** -related genes: an analysis of autopsy samples
AU Waki, Takayoshi; Tamura, Gen; Sato, Makoto; Motoyama, Teiichi
CS Department of Pathology, Yamagata University School of Medicine, Yamagata, 990-9585, Japan
SO Oncogene (2003), 22(26), 4128-4133 CODEN: ONCNES; ISSN: 0950-9232
PB Nature Publishing Group
DT Journal
LA English
AB Age-related ***methylation*** may have the potential to behave as a mutator process. To clarify the physiol. consequence of age-related ***methylation*** of ***tumor*** suppressor and ***tumor*** -related genes, the authors studied promoter ***methylation*** status in nonneoplastic cells of various organs obtained at autopsy by ***methylation*** -specific PCR. Promoter ***methylation*** status of APC, DAP-kinase, E-cadherin, GSTP1, hMLH1, ***p16*** , RASSF1A and RUNX3 genes, which are frequently silenced in certain human malignancies, was studied in nonneoplastic cells of the esophagus, ***stomach*** , small and large intestines, liver, pancreas, kidney and lung obtained from 38 Japanese autopsies. The ***tumor*** suppressor and ***tumor*** -related genes, except APC and RASSF1A, were generally unmethylated in samples obtained from people who were less than 32 yr old. ***Methylated*** promoters were present at variable frequencies in a tissue-specific manner in samples obtained from people who were greater than 42 yr old, although GSTP1 and hMLH1 ***methylation*** was absent or infrequent and lacked tissue specificity. In the majority of organs, the incidence of age-related ***methylation*** paralleled the reported ***methylation*** incidence in malignant counterparts. Thus, age-related ***methylation*** of a different set of genes is thought to constitute a field defect in different organs.
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:336015 CAPLUS <<LOGINID::20080705>>
DN 139:177695
TI Profile of Aberrant ***CpG*** Island ***Methylation*** Along the Multistep Pathway of ***Gastric*** Carcinogenesis
AU Kang, Gyeong Hoon; Lee, Sun; Kim, Jung-Sun; Jung, Hwoon-Yong
CS Department of Pathology, Seoul National University College of Medicine and Cancer Research Institute, Seoul, S. Korea
SO Laboratory Investigation (2003), 83(5), 635-641 CODEN: LAINAW; ISSN: 0023-6837
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB To date, several reports on ***methylation*** of various genes in ***gastric*** cancer (GC) were published. However, most of these studies focused on cancer tissues or a single gene only and gave no information about the ***methylation*** status of specific genes in the premalignant stages or about the concurrent ***methylation*** of other genes in specific lesions. We attempted to investigate ***methylation*** of multiple genes in a large sample collection of GC (n = 80), ***gastric*** adenoma (GA) (n = 79), intestinal metaplasia (IM) (n = 57), and chronic gastritis (CG) (n = 74). We detd. the ***methylation*** frequency of 12 genes, including APC, COX-2, DAP-kinase, E-cadherin, GSTP1, hMLH1, MGMT, ***p16*** , p14, RASSF1A, THBS1, and TIMP3 by ***methylation*** -specific PCR. Five different classes of ***methylation*** behaviors were found: (1) genes ***methylated*** in GC only (GSTP1 and RASSF1A); (2) genes showing low ***methylation*** frequency (<12%) in CG, IM, and GA, but significantly higher ***methylation*** frequency in GC (COX-2, hMLH1, and ***p16***); (3) a gene with low and similar ***methylation*** frequency (8.8-21.3%) in four-step lesions (MGMT); (4) genes with high and similar ***methylation*** frequency (53-85%) in four-step lesions (APC and E-cadherin); and (5) genes showing an increasing tendency with or without fluctuation of the ***methylation*** frequency along the progression (DAP-kinase, p14, THBS1, and TIMP3). The av. no. of ***methylated*** genes was 2.7, 3.6, 3.4, and 5.2 per 12 tested genes in CG, IM, GA, and GC, resp. Our results suggest that ***tumor*** suppressor genes show a gene type-specific ***methylation*** profile and that aberrant ***CpG*** island ***methylation*** tends to accumulate along the pathway of multistep carcinogenesis.
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:254030 CAPLUS <<LOGINID::20080705>>
DN 139:82867
TI Profile of Aberrant ***CpG*** Island ***methylation*** along multistep ***gastric*** carcinogenesis
AU Kang, Gyeong Hoon; Lee, Sun; Kim, Jung-Sun; Jung, Hwoon-Yong
CS Department of Pathology, Seoul National University College of Medicine and Cancer Research Institute, Seoul, S. Korea
SO Laboratory Investigation (2003), 83(4), 519-526 CODEN: LAINAW; ISSN: 0023-6837
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB The ***stomach*** is one of the organs whose epithelial cells frequently undergo aberrant ***methylation*** of ***CpG*** islands. To date, several reports on the ***methylation*** of various genes in ***gastric*** cancer

(GC) have been published. However, most of these studies have focused on cancer tissues or a single gene only and gave no information about the ***methylation*** status of specific genes in the premalignant stages or the concurrent ***methylation*** of other genes in specific lesions. We attempted to investigate ***methylation*** of multiple genes in a large sample collection of GC (n = 80), ***gastric*** adenoma (GA) (n = 79), intestinal metaplasia (IM) (n = 57), and chronic gastritis (CG) (n = 74). We detd. the ***methylation*** frequency of 12 genes, including APC, COX-2, DAP-kinase, E-cadherin, GSTP1, hMLH1, MGMT, ***p16*** , p14, RASSF1A, THBS1, and TIMP3, by ***methylation*** -specific PCR. Five different classes of ***methylation*** behaviors were found: (a) genes ***methylated*** in GC only (GSTP1 and RASSF1A), (b) genes showing low ***methylation*** frequency (<12%) in CG, IM, and ***gastric*** adenoma (GA) but significantly higher ***methylation*** frequency in GC (COX-2, hMLH1, ***p16***), (c) a gene with low and similar ***methylation*** frequency (8.8-21.3%) in four-step lesions (MGMT), (d) genes with high and similar ***methylation*** frequency (53-85%) in four-step lesions (APC and E-cadherin), and (e) genes showing an increasing tendency with or without fluctuation of the ***methylation*** frequency along the progression (DAP-kinase, p14, THBS1, and TIMP-3). The av. no. of ***methylated*** genes was 2.7, 3.6, 3.4, and 5.2 per 12 tested genes in CG, IM, GA, and GC, resp. Aberrant ***methylation*** at multiple loci in the same lesions suggests an overall deregulation of the ***methylation*** control, which occurs early in multistep ***gastric*** carcinogenesis. Our results suggest that ***tumor*** -suppressor genes show a gene-type specific ***methylation*** profile along the multistep carcinogenesis and that aberrant ***CpG** island ***methylation*** tend to accumulate along the multistep carcinogenesis.
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:253778 CAPLUS <<LOGINID::20080705>>
DN 138:383158
TI Global and non-random ***CpG** -island ***methylation*** in ***gastric*** ***carcinoma*** associated with Epstein-Barr virus
AU Chong, Ja-Mun; Sakuma, Kazuya; Sudo, Makoto; Ushiku, Tetsuo; Uozaki, Hiroshi; Shibahara, Junji; Nagai, Hideo; Funata, Nobuaki; Taniguchi, Hirokazu; Aburatani, Hiroyuki; Fukayama, Masashi
CS Department of Pathology, Graduate School of Medicine, The University of Tokyo, Tokyo, 113-0033, Japan
SO Cancer Science (2003), 94(1), 76-80 CODEN: CSACCM; ISSN: 1347-9032
PB Japanese Cancer Association
DT Journal
LA English
AB DNA hypermethylation may play a primary role in the genesis of Epstein-Barr virus (EBV)-assocd. ***gastric*** ***carcinoma*** (GC) (EB-VaGC). ***Methylation*** -specific PCR targeting ***CpG*** -islands demonstrated markedly increased ***methylation*** of specific genes, such as p14, p15 and ***p16*** genes, in EBVaGC in vivo. A high frequency of ***methylation*** was obsd. in an EBVaGC strain of severe combined immunodeficiency mice, and the expression of ***methylated*** genes in the strain was apparently lower than the expression of the unmethylated genes in EBV-neg. GC strains. Although over-expression of DNA ***methyltransferases*** (DNMTs) is known to be assocd. with some human cancers, real-time PCR demonstrated that DNMTs expression was suppressed in EBVaGC. The DNA ***methylation*** of specific genes, independently of DNMTs expression, may be important in the development of EBVaGC.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:49265 CAPLUS <<LOGINID::20080705>>
DN 138:383015
TI ***p16*** hypermethylation during ***gastric*** carcinogenesis of Wistar rats by N- ***methyl*** -N'-nitro-N-nitrosoguanidine
AU Bai, Hua; Gu, Liankun; Zhou, Jing; Deng, Dajun
CS Department of Cancer Etiology, Peking University Health Science Center and Beijing Institute for Cancer Research, Beijing, 100034, Peop. Rep. China
SO Mutation Research, Genetic Toxicology and Environmental Mutagenesis (2003), 535(1), 73-78 CODEN: MRGMFI; ISSN: 1383-5718
PB Elsevier B.V.
DT Journal
LA English
AB Inactivation of the ***tumor*** suppressor gene, ***p16*** by ***CpG*** hypermethylation is a common event in various ***tumors*** including ***gastric*** ***carcinoma*** . The aim of this study is to investigate if ***p16*** hypermethylation is an early and frequent event in ***gastric*** carcinogenesis induced by N- ***methyl*** -N'-nitro-N-nitrosoguanidine (MNNG). The frequency and timing of ***p16*** hypermethylation during the multistep ***gastric*** carcinogenesis in Wistar rats were analyzed in various microdissected ***gastric*** lesions. The ***p16*** ***methylation*** status and the presence of ***p16*** protein were analyzed by ***methylation*** -specific PCR and immunohistochem., resp. Results showed that ***p16*** ***methylation*** frequency was correlated with the severity of ***gastric*** pathol. lesions, pos. For instance, ***p16*** ***methylation*** was found in 2.7% of normal ***gastric*** epithelium (n=36), 16.7% of chronic atrophy gastritis (n=24), 37.5% of ***dysplasia*** (n=24), 67.4% of ***gastric*** adenoma (n=43), and 85.2% of ***gastric*** ***carcinoma*** (n=27). The ***p16*** ***methylation*** in the distal ***stomach*** epithelium was higher than that in the proximal ***stomach*** ***p16*** protein was expressed in all of 15 ***p16*** unmethylated ***gastric*** epithelial samples, but not expressed in all of 12 ***p16*** ***methylated*** samples. These results suggest that ***CpG*** island hypermethylation may account for the silencing of ***p16*** in rat ***stomach*** and is an early event whose accumulation will finally lead to ***gastric*** carcinogenesis.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:9764 CAPLUS <<LOGINID::20080705>>
DN 138:252629
TI ***P16*** hypermethylation contributes to the characterization of gene inactivation profiles in primary ***gastric*** cancer

AU Ficorella, Corrado; Cannita, Katia; Ricevuto, Enrico; Toniato, Elena; Fusco, Carlo; Sinopoli, Nuntia Teresa; De Galitiis, Federica; Di Rocco, Zorika Christiana; Porzio, G.; Frati, Luigi; Gulino, Alberto; Martinotti, Stefano; Marchetti, Paolo
CS Department of Experimental Medicine, University of L'Aquila, L'Aquila, I-67100, Italy
SO Oncology Reports (2003), 10(1), 169-173 CODEN: ORPEW; ISSN: 1021-335X
PB Oncology Reports
DT Journal
LA English
AB The objective of this study was to investigate the contribution of ***p16*** inactivation in ***gastric*** cancer and to compare it with p53. A cohort of 34 primary GCs were analyzed for ***p16*** mutations and transcriptional silencing of the gene due to hypermethylation of the promoter. SSCP anal. and direct sequencing of exons 1 and 2 of the ***p16*** gene were performed to detect any structural alterations. The ***methylation*** specific PCR (MSP) assay was applied to reveal hypermethylation of the ' ***CpG*** ' island in the regulatory region using specific primer pairs for ***methylated*** and unmethylated nucleotides after a chem. reaction converting cytosines into uracile when unmethylated. SSCP and direct sequencing anal. did not detect any ***p16*** mutations. The MSP assay showed 4 MSP+ variants (11.8%). Three MSP+ were stage III-IV disease and 1 MSP+ was detected in an early stage disease (IB). All MSP+ were diffuse type adenocarcinomas. The MSP+ samples were different from previously reported samples harboring p53 mutations in the same cohort. These data increase the no. of ***gastric*** cancers showing alterations of either p53 or ***p16*** to 29.4% (10/34). Functional inactivation by hypermethylation of the ***p16*** locus and p53 mutations could play a significant, complementary role in the pathogenesis of sporadic ***gastric*** cancer.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2002:713773 CAPLUS <<LOGINID::20080705>>
DN 138:2963
TI Promoter ***methylation*** status of E-cadherin, hMLH1, and ***p16*** genes in nonneoplastic ***gastric*** epithelia
AU Waki, Takayoshi; Tamura, Gen; Tsuchiya, Takashi; Sato, Kiyoshi; Nishizuka, Satoshi; Motoyama, Teiichi
CS Department of Pathology, Yamagata University School of Medicine, Yamagata, Japan
SO American Journal of Pathology (2002), 161(2), 399-403 CODEN: AJPAA4; ISSN: 0002-9440
PB American Society for Investigative Pathology
DT Journal
LA English
AB Silencing of ***tumor*** suppressor and ***tumor*** -related genes by hypermethylation at promoter ***CpG*** islands is one of the major events in human ***tumorigenesis*** . Promoter ***methylation*** is also present in nonneoplastic cells as an age-related tissue-specific phenomenon that precedes the development of ***neoplasia*** . To clarify the significance of promoter ***methylation*** in nonneoplastic ***gastric*** epithelia as a precancerous signal, we investigated promoter ***methylation*** status of E-cadherin, hMLH1, and ***p16*** genes in nonneoplastic cells of various organs obtained at autopsy, and compared the results with those of nonneoplastic epithelia of a cancerous ***stomach*** . ***Methylation*** of these genes was not seen in nonneoplastic cells of organs from people who were 22 yr and younger (0%, 0 of 6). In contrast, E-cadherin and ***p16*** were ***methylated*** in nonneoplastic ***gastric*** epithelia of persons who were 45 yr or older. The nos. were 86% (12 of 14) and 29% (4 of 14), resp. E-cadherin ***methylation*** occurred preferentially in the intestines, whereas ***p16*** ***methylation*** was almost restricted to the ***stomach*** . For samples obtained from patients with ***stomach*** cancer, ***methylation*** was frequently obsd. in both ***neoplastic*** and corresponding nonneoplastic ***gastric*** epithelia: 47% (44 of 94) and 67% (63 of 94) for E-cadherin, 32% (30 of 94) and 24% (23 of 94) for hMLH1, and 22% (21 of 94) and 44% (41 of 94) for ***p16*** , resp. hMLH1 ***methylation*** was not seen in nonneoplastic ***gastric*** epithelia from autopsy samples but occurred significantly in samples from nonneoplastic tissues of individuals with ***stomach*** cancer. Therefore, detection of hMLH1 ***methylation*** in nonneoplastic ***gastric*** epithelia may be useful for screening patients who may be at risk of developing ***gastric*** cancer.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2002:243536 CAPLUS <<LOGINID::20080705>>
DN 137:214494
TI Epstein-Barr virus-positive ***gastric*** ***carcinoma*** demonstrates frequent aberrant ***methylation*** of multiple genes and constitutes ***CpG*** island ***methylator*** phenotype-positive ***gastric*** ***carcinoma***
AU Kang, Gyeong Hoon; Lee, Sun; Kim, Woo Ho; Lee, Hye Won; Kim, Jin Cheon; Rhyu, Mun-Gan; Ro, Jae Y.
CS Department of Pathology, Seoul National University College of Medicine and Cancer Research Institute, Seoul, 110-744, S. Korea
SO American Journal of Pathology (2002), 160(3), 787-794 CODEN: AJPAA4; ISSN: 0002-9440
PB American Society for Investigative Pathology
DT Journal
LA English
AB ***CpG*** island ***methylation*** is an important mechanism for inactivating the genes involved in ***tumorigenesis*** . ***Gastric*** ***carcinoma*** (GC) is one of the ***tumors*** that exhibits a high frequency of aberrant ***CpG*** island ***methylation*** . There have been many reports suggesting a close link between Epstein-Barr virus (EBV) and the development of GC. However, little is known about the oncogenic mechanism of EBV in ***gastric*** carcinogenesis. Twenty-one cases of EBV-pos. GC and 56 cases of EBV-neg. GC were examd. for aberrant DNA ***methylation*** of the ***CpG*** islands of 19 genes or loci and the differences in the ***methylation*** frequency between EBV-pos. and -neg. GCs were investigated to det. a role of aberrant ***methylation*** in EBV-related ***gastric*** carcinogenesis. The av. no. of ***methylated*** genes or loci was higher in EBV-pos. GCs than in EBV-neg. GCs (13.4 vs. 7.8, resp., $P < 0.001$). EBV-pos. GCs showed ***methylation*** in at least 10 ***CpG*** islands (52.6% of the tested genes), whereas 62.5% of EBV-neg. GCs showed ***methylation*** in <10 ***CpG*** islands. THBS1, APC, ***p16*** , 14-3-3 sigma, MINT1, and MINT25 were

methylated at a frequency > 90% in EBV-pos. GCs. The ***methylation*** frequency difference in the resp. ***CpG*** islands between EBV-pos. and -neg. GCs was statistically significant (P < 0.05). Among these genes or loci, the ***methylation*** frequency of ***p16*** in the EBV-pos. GCs was more than three times higher than in the EBV-neg. GCs. The PTEN, RASSF1A, GSTP1, MGMT, and MINT2 were ***methylated*** in EBV-pos. GCs at a frequency of more than three times that of the EBV-neg. GCs. These results demonstrate a relationship between EBV and aberrant ***methylation*** in GC and suggest that aberrant ***methylation*** may be an important mechanism of EBV-related ***gastric*** carcinogenesis.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:584392 CAPLUS <<LOGINID::20080705>>
DN 135:270997
TI ***Tumor*** suppressor genes in the 9p21 gene cluster are selective targets of inactivation in neuroendocrine gastroenteropancreatic ***tumors***
AU Lubomierski, Nikolaus; Kersting, Michael; Bert, Tillmann; Muench, Karin; Wulbrand, Ulrich; Schuermann, Marcus; Bartsch, Detlev; Simon, Babette
CS Department of Internal Medicine, Divisions of Gastroenterology, Philipps-University Marburg, Marburg, 35033, Germany
SO Cancer Research (2001), 61(15), 5905-5910 CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Functional inactivation of the Rb and p53 pathways appears to be a rite of passage for all cancerous cells. However, p53 and Rb alterations are rare events in neuroendocrine gastroenteropancreatic (GEP) ***tumors***. The CDKN2 locus on chromosome 9p21 sits at the nexus of both pathways harboring ***tumor*** suppressor genes, which restrain cell growth by affecting the function of pRb and p53. Therefore, the authors analyzed the implication of their inactivation in 37 primary neuroendocrine GEP ***tumors*** and two cell culture models. RT-PCR anal. revealed loss of expression of at least one of the ***tumor*** suppressor genes CDKN2A/***p16***, CDKN2B/p15, and CDKN2D/p14 with distinct genetic profiles, most frequently in nonfunctional pancreatic ***tumors*** (57%) and small intestinal carcinoids (44%), and less commonly in insulinomas (30%) and gastrinomas (22%). DNA anal. and ***methylation*** -specific PCR attributed loss of expression to either homozygous deletion or 5' ***CpG*** island hypermethylation. 5-Aza-2-deoxycytidine treatment reversed CDKN2A/***p16*** and CDKN2B/p15 silencing with concurrent growth restraint. Thus, ***tumor*** suppressor genes localized in the 9p21 gene cluster are specific targets of inactivation in neuroendocrine GEP ***tumors***, and demethylating agents might hold promise for selective therapy.
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:507427 CAPLUS <<LOGINID::20080705>>
DN 136:116309
TI Concurrent hypermethylation of multiple ***tumor*** -related genes in ***gastric*** ***carcinoma*** and adjacent normal tissues
AU Leung, Wai K.; Yu, Jun; Ng, Enders K. W.; To, Ka Fai; Ma, Po K.; Lee, Tin Lap; Go, Minnie Y. Y.; Chung, S. C. Sydney; Sung, Joseph J. Y.
CS Department of Medicine & Therapeutics, Prince of Wales Hospital, Chinese University of Hong Kong, Shatin, Hong Kong
SO Cancer (New York, NY, United States) (2001), 91(12), 2294-2301 CODEN: CANCAR; ISSN: 0008-543X
PB John Wiley & Sons, Inc.
DT Journal
LA English
AB Transcriptional silencing by ***CpG*** -island hypermethylation now is believed to be an important mechanism of ***tumorigenesis***. To date, studies on ***CpG*** -island hypermethylation in ***gastric*** ***carcinoma*** and adjacent normal tissues are few. The authors examd. 5 ***gastric*** ***carcinoma*** cell lines, 26 frozen ***gastric*** ***carcinoma*** tissues and their adjacent nontumor area for concurrent ***CpG*** -island hypermethylation in 6 ***tumor*** -related genes (p15, ***p16***, E-cadherin, GST-pi, hMLH1 and VHL) by ***methylation*** -specific PCR. Nontumorous ***gastric*** tissues from 10 gastritis patients were used as controls. Hypermethylation was not detected in any tissue taken from gastritis patients but was identified in all 5 cell lines and in 24 (92.3%) ***gastric*** ***carcinoma*** patients. ***CpG*** -island ***methylation*** in ***tumor*** -related genes also was detected in 7 out of the 25 adjacent normal tissues from cancer patients. Hypermethylation of E-cadherin, p15, and ***p16*** were detected more frequently than GST-pi and hMLH1, whereas aberrant ***methylation*** of VHL was not detected. Concurrent hypermethylation in 2 or more ***tumor*** -related genes was detected in 3 out of the 5 ***gastric*** ***carcinoma*** cell lines, 22 (84.6%) ***tumor*** samples, and 5 (20%) adjacent ***gastric*** tissues. 18 (69.2%) ***Tumor*** samples showed hypermethylation in .gtoreq. 3 genes. The current study showed that concurrent hypermethylation of multiple ***tumor*** -related genes is detected frequently in ***gastric*** ***carcinoma*** and adjacent normal tissues. Study findings suggested that a mechanism that leads to dysregulation in ***CpG*** -island ***methylation*** is likely to be involved in the early ***gastric*** carcinogenesis process.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:295890 CAPLUS <<LOGINID::20080705>>
DN 135:44434
TI ***CpG*** island ***methylation*** in premalignant stages of ***gastric*** ***carcinoma***
AU Kang, Gyeong Hoon; Shim, Yhong-Hee; Jung, Hwoon-Yong; Kim, Woo Ho; Ro, Jae Y.; Rhyu, Mun-Gan
CS Department of Pathology, Seoul National University College of Medicine and Cancer Research Institute, Seoul, 110-744, S. Korea
SO Cancer Research (2001), 61(7), 2847-2851 CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB There are limited reports on ***methylation*** anal. of the premalignant lesions of ***gastric*** ***carcinoma***

thus far. This is despite the fact that ***gastric*** ***carcinoma*** is one of the ***tumors*** with a high frequency of ***CpG** island hypermethylation. To det. the frequency and timing of hypermethylation during multistep ***gastric*** carcinogenesis, non- ***neoplastic*** ***gastric*** mucosa, chronic gastritis, intestinal metaplasia, adenomas, and ***carcinomas*** were analyzed for their ***p16*** human Mut L homolog 1 (hMLH1), death-assocd. protein (DAP)-kinase, thrombospondin-1 (THBS1), and tissue inhibitor of metalloproteinase 3 (TIMP-3) ***methylation*** status using ***methylation*** -specific PCR. Three different classes of ***methylation** behaviors were found in the five tested genes. DAP-kinase was ***methylated** at a similar frequency in all four stages, whereas hMLH1 and ***p16*** were ***methylated*** in cancer samples (20.3% and 42.2%, resp.) more frequently than in intestinal metaplasia (6.3% and 2.1%, resp.) or adenomas (9.8% and 11.5%, resp.). However, hMLH1 and ***p16*** were not ***methylated** in chronic gastritis. THBS-1 and TIMP-3 were ***methylated** in all stages but showed a marked increase in hypermethylation frequency from chronic gastritis (10.1% and 14.5%, resp.) to intestinal metaplasia (34.7% and 36.7%, resp.) and from adenomas (28.3% and 26.7%, resp.) to ***carcinomas*** (48.4% and 57.4%, resp.). The hMLH1, THBS1, and TIMP-3 hypermethylation frequencies were similar in both intestinal metaplasia and adenomas, but the ***p16*** hypermethylation frequency tended to be higher in adenomas (11.5%) than in intestinal metaplasia (2.1%). The av. no. of ***methylated** genes was 0.6, 1.1, 1.1, and 2.0 per five genes per sample in chronic gastritis, intestinal metaplasia, adenomas, and ***carcinomas*** , resp. This shows a marked increase in ***methylated** genes from non-metaplastic mucosa to intestinal metaplasia as well as from premalignant lesions to ***carcinomas*** . These results suggest that ***CpG*** island hypermethylation occur early in multistep ***gastric*** carcinogenesis and tend to accumulate along the multistep carcinogenesis.
RE CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:82605 CAPLUS <<LOGINID::20080705>>
DN 135:32043
TI DNA ***methyltransferase*** expression and DNA ***methylation*** of ***CPG** islands and peri-centromeric satellite regions in human colorectal and ***stomach*** cancers
AU Kanai, Yae; Ushijima, Saori; Kondo, Yutaka; Nakanishi, Yukihiro; Hirohashi, Setsuo
CS Pathology Division, National Cancer Center Research Institute, Tokyo, 104-0045, Japan
SO International Journal of Cancer (2001), 91(2), 205-212
CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss, Inc.
DT Journal
LA English
AB The authors evaluated the significance of aberrant DNA ***methyltransferase*** expression in human carcinogenesis by examg. 32 colorectal and 34 ***stomach*** cancers. Levels of mRNAs encoding DNA ***methyltransferases** were measured by reverse transcription, followed by real-time quant. detection of PCR products. The DNA ***methylation*** state of ***CpG** islands and peri-centromeric satellite regions was examd. by bisulfite modification and Southern blotting, resp. The av. level of mRNA for DNMT1 and DNMT3b in colorectal and ***stomach*** cancers was significantly higher than in corresponding non-cancerous mucosae, whereas the av. level of mRNA for DNMT2 was significantly lower in colorectal and ***stomach*** cancers than in non-cancerous tissue. Over-expression of DNMT3b in ***stomach*** cancer was significantly higher in cases with lymph node metastasis than in cases without. DNA hypermethylation on the ***p16*** , human Mut L homolog-1 and thrombospondin-1 genes and the ***methylated*** in ***tumor*** (MINT) 1, 2, 12, 25 and 31 clones was found in 23%, 27%, 9%, 23%, 20%, 23%, 20% and 10% of the colon cancers and in 9%, 19%, 30%, 25%, 34%, 19%, 81% and 3% of the ***stomach*** cancers, resp. Criteria for identification of the ***CpG** island ***methylator*** phenotype (CIMP) were met in 23% of colorectal cancers and 31% of ***stomach*** cancers. DNA hypomethylation on satellites 2 and 3 was detected in 0% and 8% of colorectal and ***stomach*** cancers, resp. Over-expression of DNMT1 mRNA was significantly assocd. with CIMP, whereas the level of DNMT3b mRNA was not assocd. with CIMP or DNA hypomethylation of pericentromeric satellite regions. These data suggest that both over-expression of the maintenance DNA ***methyltransferase*** DNMT1 and over-expression of a newly identified de novo DNA ***methyltransferase*** , DNMT3b, are involved in human carcinogenesis, probably at different stages and through different mechanisms.
RE CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:509838 CAPLUS <<LOGINID::20080705>>
DN 134:3300
TI ***Methylation*** of specific ***CpG** sites in the promoter region could significantly down-regulate p16INK4a expression in ***gastric** adenocarcinoma
AU Song, Sang Hyun; Jong, Hyun-Soon; Choi, Hyun Ho; Kang, Shin Hyeok; Ryu, Min Hee; Kim, Noe Kyeong; Kim, Woo-Ho; Bang, Yung-Jue
CS Cancer Research Center, Seoul National University College of Medicine., Seoul, S. Korea
SO International Journal of Cancer (2000), 87(2), 236-240
CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Silencing of p16INK4a by ***methylation*** of the ***CpG** islands in the promoter region was found to be an alternative mechanism of inactivation in several ***tumors*** . However, in ***gastric*** ***carcinoma*** , the relationship between ***methylation*** status and the transcriptional silencing of the ***p16*** gene remains to be clarified. In this study, the authors investigated whether ***methylation*** of a few specific ***CpG** sites in the promoter region could significantly down-regulate ***p16*** activity in the ***tumorigenesis*** of ***gastric*** ***carcinoma** . By Southern anal. and bisulfite-modified genomic sequencing of 9 ***gastric** - ***carcinoma*** cell lines, we found that the 5 cell lines (55.5%) not expressing ***p16*** mRNA had ***methylated** ***CpG** sites at the promoter region of ***p16*** . In addn., we analyzed the ***p16*** -protein expression of 28 primary ***gastric*** ***carcinomas** and their normal counterparts by immunohistochem. staining (IHC) on paraffin sections. Loss of ***p16*** expression was detected in 6 cases (22%). In 5 out of these 6 (83%), the actual ***p16***

gene was inactivated by de novo ***methylation*** of the promoter sites. Taken together, these results suggest a strong correlation between de novo ***methylation*** of a few specific ***CpG*** sites and transcriptional silencing of the ***p16*** gene is ***gastric*** ***carcinoma*** .
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:415066 CAPLUS <<LOGINID::20080705>>
DN 133:294376
TI Correlation of ***p16*** hypermethylation with ***p16*** protein loss in sporadic ***gastric*** ***carcinomas***
AU Shim, Yhong-Hee; Kang, Gyeong Hoon; Ro, Jae Y.
CS Molecular Pathology Laboratory, University of Ulsan, Seoul, 138-736, S. Korea
SO Laboratory Investigation (2000), 80(5), 689-695 CODEN: LAINAW; ISSN: 0023-6837
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Hypermethylation of ***p16*** has been detected frequently in a variety of cancer cells and is known to repress the level of ***p16*** transcription. In human ***gastric*** ***carcinoma*** (GC) cells, ***p16*** protein loss has often been detected, but genetic alterations of ***p16*** are infrequent. To investigate the mol. mechanism of ***p16*** gene inactivation in ***gastric*** carcinogenesis, we examd. the ***methylation*** status of ***p16*** in GC using ***methylation*** -specific PCR. Thirty-seven of eighty-eight (42%) GC showed ***p16*** hypermethylation. Immunohistochem. anal. of 41 cases of GC showed a complete loss of ***p16*** immunoreactivity in 19 of 22 (86%) ***methylation*** -pos. cases, but in only 2 of 19 (11%) ***methylation*** -neg. cases. Of 88 GC, 21 cases were previously identified as having microsatellite instability (MSI). Interestingly, 13 of 21 (62%) MSI-pos. ***tumors*** and 24 of 67 (36%) MSI-neg. ***tumors*** had hypermethylation on ***p16*** . The relatively high frequency of hypermethylation on ***p16*** and the strong correlation between the immunoreactivity and ***methylation*** patterns suggest that ***methylation*** is an important mechanism for ***p16*** gene inactivation in GC.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1999:725082 CAPLUS <<LOGINID::20080705>>
DN 132:48358
TI Aberrant ***methylation*** in ***gastric*** cancer associated with the ***CpG*** island ***methylator*** phenotype
AU Toyota, Minoru; Ahuja, Nita; Suzuki, Hiromu; Itoh, Fumio; Ohe-Toyota, Mutsumi; Imai, Kohzoh; Baylin, Stephen B.; Issa, Jean-Pierre J.
CS The Johns Hopkins Oncology Center, Baltimore, MD, 21231, USA
SO Cancer Research (1999), 59(21), 5438-5442 CODEN: CNREA8; ISSN: 0008-5472
PB AACR Subscription Office
DT Journal
LA English
AB Aberrant ***methylation*** of 5' ***CpG*** islands is thought to play an important role in the inactivation of ***tumor*** suppressor genes in cancer. In colorectal cancer, a group of ***tumors*** is characterized by a hypermethylator phenotype termed ***CpG*** island ***methylator*** phenotype (CIMP), which includes ***methylation*** of such genes as ***p16*** and hMLH1. To study whether CIMP is present in ***gastric*** cancer, the ***methylation*** status of five newly cloned ***CpG*** islands was examd. in 56 ***gastric*** cancers using bisulfite-PCR. Simultaneous ***methylation*** of three loci or more was obsd. in 23 (41%) of 56 cancers, which suggests that these ***tumors*** have the hypermethylator phenotype CIMP. There was a significant concordance between CIMP and the ***methylation*** of known genes including ***p16*** , and hMLH1; ***methylation*** of ***p16*** was detected in 16 (70%) of 23 CIMP+ ***tumors*** , 1 (8%) of 12 CIMP intermediate ***tumors*** , and 1 (5%) of 21 CIMP- ***tumors*** . ***Methylation*** of the hMLH1 gene was detected in three of five ***tumors*** that showed microsatellite instability, and all three of the cases were CIMP+. The CIMP phenotype is an early event in ***gastric*** cancer, being present in the normal tissue adjacent to cancer in 5 of 56 cases. These results suggest that CIMP may be one of the major pathways that contribute to ***tumorigenesis*** in ***gastric*** cancers.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1999:703642 CAPLUS <<LOGINID::20080705>>
DN 132:164378
TI Distinct ***methylation*** pattern and microsatellite instability in sporadic ***gastric*** cancer
AU Suzuki, Hiromu; Itoh, Fumio; Toyota, Minoru; Kikuchi, Takefumi; Kakiuchi, Hideki; Hinoda, Yuji; Imai, Kohzoh
CS First Department of Internal Medicine, Sapporo Medical University, Sapporo, 060-8543, Japan
SO International Journal of Cancer (1999), 83(3), 309-313 CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Aberrant 5' ***CpG*** island ***methylation*** is an alternative mechanism of gene inactivation during the development of cancer as demonstrated for several ***tumor*** -suppressor genes. Also, marked relation of microsatellite instability (MSI) and DNA ***methylation*** has been reported in sporadic colorectal cancer, which is a result of epigenetic inactivation of hMLHI in assocn. of promoter hypermethylation. In the present study, the authors investigated the 5' ***CpG*** island hypermethylation of hMLHI, E-cadherin and ***p16*** in 61 primary ***gastric*** cancers (GCs) by using combined bisulfite restriction anal. (COBRA) and ***methylation*** -specific PCR (MSP), and their MSI status. Of 61 GCs investigated, 5 (8.1%) ***tumors*** presented hMLHI ***methylation*** , 16 (26.2%) and 25 (40.9%) showed E-cadherin and ***p16*** ***methylation*** resp., and 8 (13.1%) presented high-frequency MSI (MSI-H). Of the 8 MSI-H patients, 5 presented hMLHI ***methylation*** , whereas no low-frequency MSI (MSI-L) and microsatellite stable (MSS) cases exhibited hMLHI ***methylation*** (5/8 vs. 0/43). Furthermore, these patients also presented E-cadherin and ***p16*** hypermethylation. The data showed a significant correlation between hMLHI

methylation and MSI in GC, and suggested that a common mechanism of aberrant de novo ***methylation*** can be postulated in these cancers.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1997:768367 CAPLUS <<LOGINID::20080705>>
DN 128:33100
OREF 128:6477a,6480a
TI Alterations of p16INK4A and p15INK4B genes in ***gastric*** ***carcinomas***
AU Lee, Young Y.; Kang, Shin H.; Seo, Jin Y.; Jung, Chui W.; Lee, Kuhn U.; Choe, Kuk J.; Kim, Byoung K.; Kim, Noe K.; Koeffler, H. Phillip; Bang, Yong-Jue
CS Department of Internal Medicine, Han Yang University School of Medicine, Seoul, S. Korea
SO Cancer (New York) (1997), 80(10), 1889-1896 CODEN: CANCAR; ISSN: 0008-543X
PB Wiley
DT Journal
LA English
AB It has been suggested that cyclin-dependent kinase inhibitors (CDKIs), including ***p16*** and p15, are ***tumor*** suppressor genes. Alterations of CDKIs have been found in most types of cancer. However, little is known about the status of ***p16*** and p15 genes, including ***methylation*** of the promoter, region, in ***gastric*** ***carcinoma***. Thirty-six primary ***gastric*** ***tumors*** and 9 ***gastric*** ***carcinoma*** cell lines were examd. for alterations of the ***p16*** and p15 genes. Deletion of the ***p16*** and p15 genes was assessed by Southern blot anal., expression by Northern blot anal., and mutation by polymerase chain reaction-single strand conformation polymorphism followed by direct sequencing. The ***methylation*** status of the 5' ***CpG*** island of the ***p16*** gene was evaluated using ***methylation*** -sensitive restriction enzymes, and reversal of the transcriptional block of the ***p16*** gene was detd. by Northern blot anal. after treatment with 5-aza-2'-deoxycytidine. Homozygous deletions of the ***p16*** and 15 genes from 2 of 9 ***gastric*** ***carcinoma*** cell lines were found. In contrast, no deletions were detected in 36 primary ***gastric*** ***tumors***, and one primary ***tumor*** showed rearrangements of the ***p16*** and p15 genes. Two ***gastric*** ***carcinoma*** cell lines showed a point mutation and an insertional mutation of the ***p16*** gene, resp.; however, no point mutations were noted for the ***p16*** and p15 genes in any of the primary ***gastric*** ***tumors***. Constitutive levels of ***p16*** mRNA expression in ***gastric*** ***carcinoma*** cell lines were quite heterogeneous; four ***gastric*** ***carcinoma*** cell lines had no detectable ***p16*** mRNA and 6 ***gastric*** ***carcinoma*** cell lines had negligible expression of p15 mRNA. Of 10 primary ***gastric*** ***tumors***, only 1 ***tumor*** expressed ***p16*** mRNA. Furthermore, abnormal DNA ***methylation*** patterns of the ***p16*** gene were found in 2 ***gastric*** ***carcinoma*** cell lines through the use of ***methylation*** -sensitive restriction enzymes. These cell lines lacked expression of ***p16*** mRNA without deletions of the ***p16*** gene. These transcriptional blocks were reversed by treatment with 5-aza-2'-deoxycytidine. Deletions of mutations of the ***p16*** and p15 genes are uncommon in primary ***gastric*** ***carcinomas***. However, defective mRNA transcription, sometimes by aberrant DNA ***methylation***, might be one of the pathways of inactivation of the ***p16*** gene that leads to the development of ***gastric*** ***carcinoma***.
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 15:38:18 ON 05 JUL 2008)
FILE 'CAPLUS' ENTERED AT 15:38:41 ON 05 JUL 2008
L1 343 S (CPG AND METHYL? AND (GASTRIC? OR STOMACH?) AND (CANCER? OR
L2 316 S L1 NOT 2008/PY
L3 264 S L2 NOT 2007/PY
L4 212 S L3 NOT 2006/PY
L5 172 S L4 NOT 2005/PY
L6 121 S L5 NOT 2004/PY
L7 5236 S P16/BI,AB
L8 19 S L6 AND L7

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FULL ESTIMATED COST 114.45 114.66

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION
CA SUBSCRIBER PRICE -15.20 -15.20

STN INTERNATIONAL LOGOFF AT 15:40:55 ON 05 JUL 2008